Effectiveness of an Analog of Thyrotropin-Releasing Hormone in Alleviating PTSD, Using an Animal Model of Anxiety

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This study looked at the potential effectiveness of pGLU-GLU-PRO-NH2 (EEP) as a treatment for PTSD in an animal model. EEP is a one amino acid substitution of the naturally occurring thyroptropin-releasing hormone (TRH, pGLU-HIS-PRO-NH2) produced in the hippocampus and surrounding limbic areas. This study attempted to connect previous studies on the potential effects of EEP on depression to the potential effects of EEP on PTSD. For this study 15 C57BL/6 mice (6 male and 9 female) were used as test subjects. A rectangular open field with a grid floor was used to measure the time spent in grid sectors against a wall relative to the time spent in the center of the apparatus. A greater amount of time spent in the center sectors was used as an operational definition of a reduction in anxiety since mice are generally thigmotaxic. Total number of grid sectors crossed was used as a measure of non-specific elevation in arousal/locomotor activity. No statistical difference between groups was found for thigmotaxis during the first minute, number of fecal bolus, or presence of fecal boli. The small sample sizes rendered the study statistically under powered.

1. Introduction

This study looked at the potential effectiveness of pGLU-GLU-PRO-NH2 (EEP) as a treatment for PTSD in an animal model. Recently there have been studies done suggesting that thyroptropin-releasing hormone (TRH) plays a role in the development and subsequent treatment of depression (Lloyd, Pekary, Sattin, & Amundson, 2001). EEP is very similar to the naturally occurring thyroptropin-releasing hormone (TRH) produced in the hippocampus and surrounding areas. Shrinking of the hippocampus occurs in individuals with PTSD and depression (McEwen, 2003). Similar areas of the brain are affected in both illnesses, which may explain their co-morbidity (Breslau, N., Davis, G., Peterson, E., & Shultz, L., 2000). An analogous tri-peptide EEP has been demonstrated to have an effect in the Forced Swim Test model of antidepressant

effect (Lloyd et al, 2001), and is resistant to rapid breakdown. This study attempted to establish a connection between previous studies on the effects of EEP on depression with possible effects of EEP on PTSD.

2. Research Methodology

For this study 15 C57BL/6 (6 male and 9 female) were used as test subjects. Half were given a dose of EEP (0.5 mg/kg) intraperitoneal (ip), while the remaining half was given the vehicle (sterile saline solution). They were then placed individually in the center of a 20 inch by 20 inch gridded enclosure for five minutes. A 100 watt equivalent florescent light pointed directly downwards, 27 inches away from the bottom of the container, shining evenly throughout. This apparatus was used to measure the time spent in grid sectors against a wall relative to the time spent in the center of the apparatus. A greater amount of time spent in the center sector was used as the operational definition of a reduction in anxiety since mice are generally thigmotaxic. Total number of grid sectors crossed was used as a measure of non-specific elevation in arousal/locomotor activity. Fecal bolus production was also used as a measure of anxiety.

3. Results

No statistical differences between the groups were found for thigmotaxis during the first minute of observation ($p= 0.51$), number of fecal bolus ($p=0.295$), or presence of fecal boli ($p=0.10$).

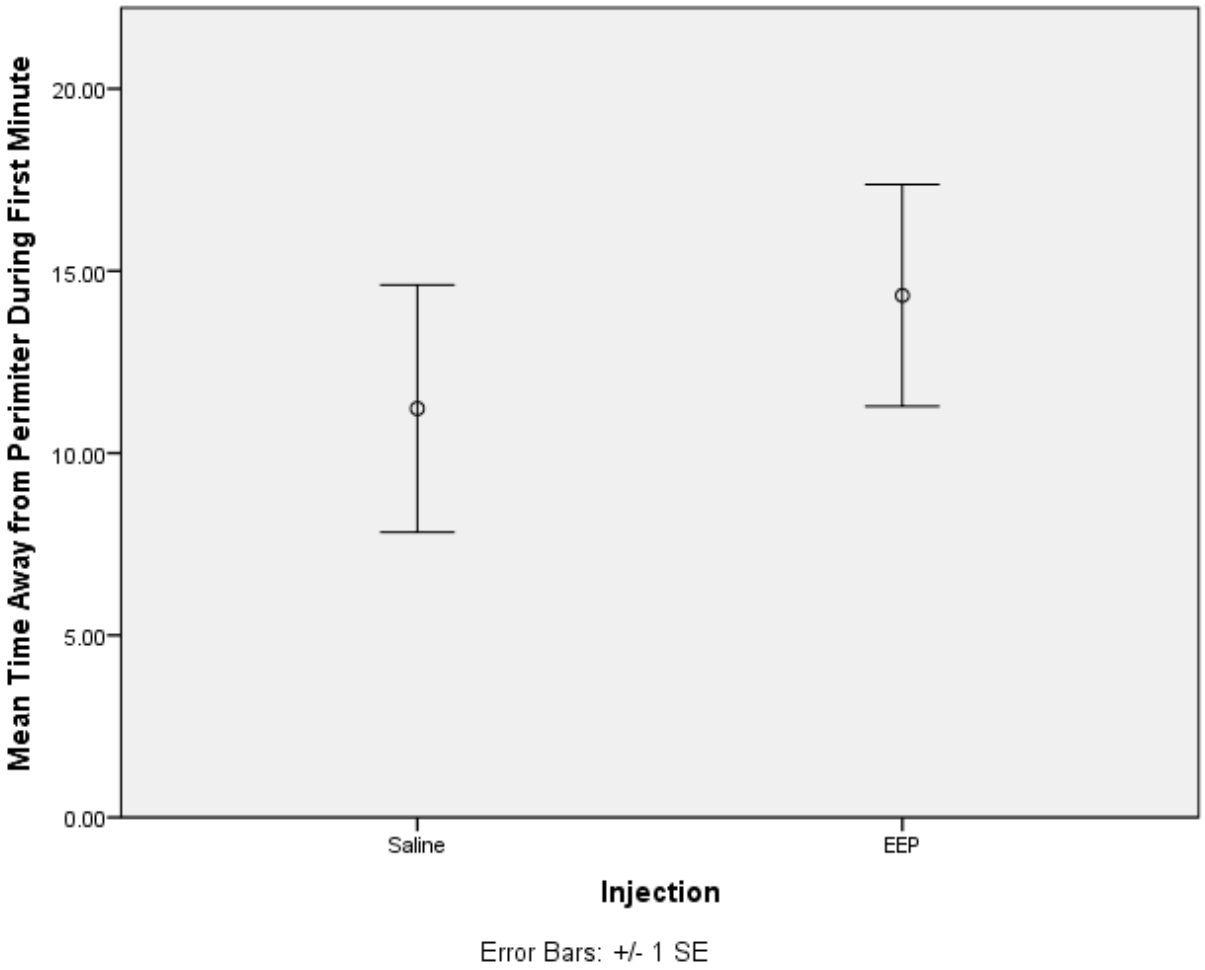

Figure 1. Amount of time that mice spent near center of apparatus (away from perimeter) after injection of either saline or EEP.

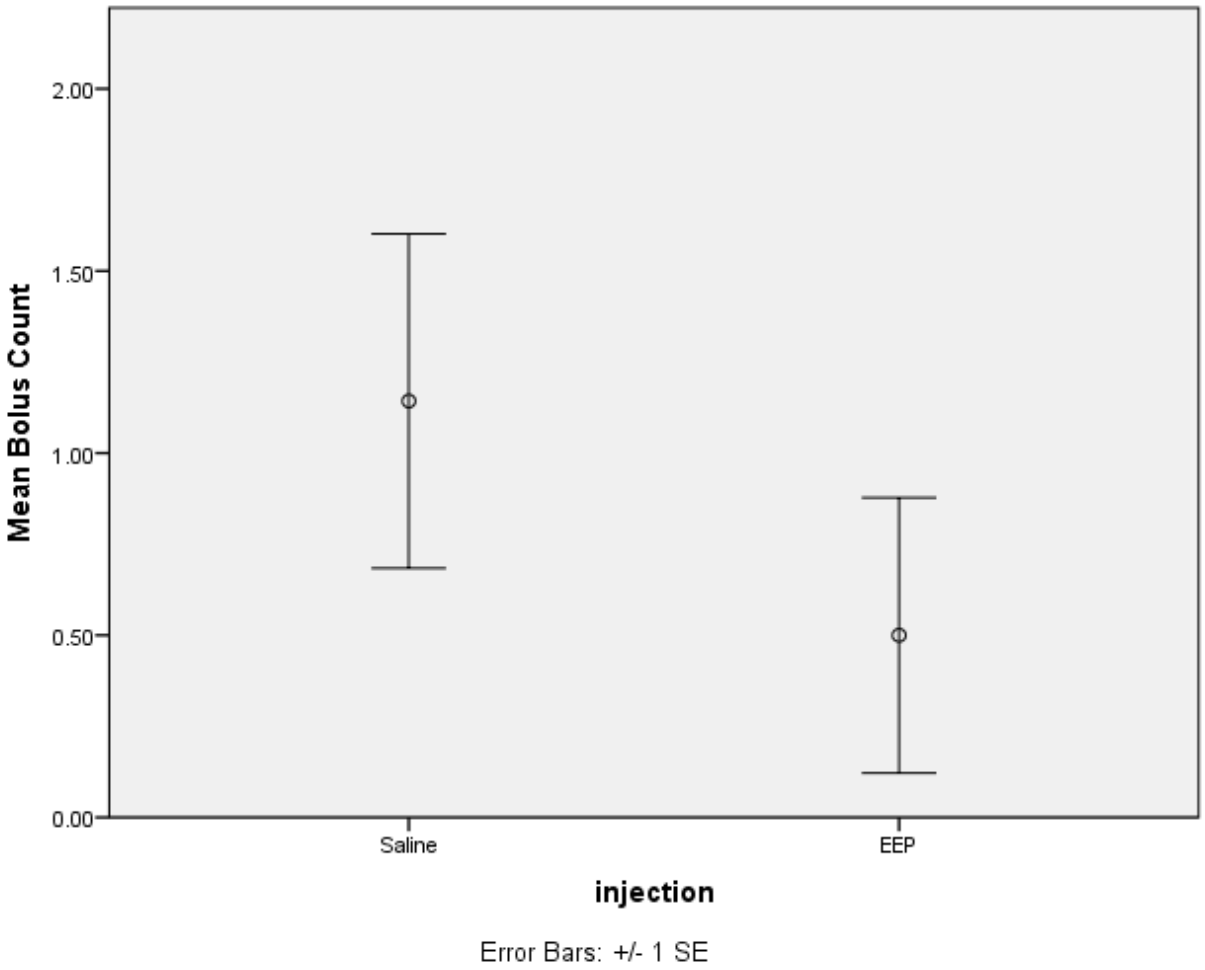

Figure 2. Mean fecal bolus count in mice after injection of either saline or EEP.

4. Discussion

The small sample sizes rendered the study statistically under powered. In addition, variation in sex of animal, and variation in the estrus status of the female animals, may have contributed to spontaneous variability and a loss of statistical power. However, the lack of effect size of thigmotaxis during the first minute of observation ($p=0.51$, partial eta-square=0.035) indicates that, if EEP does have anxiolytic properties, a larger dose would be needed. On the other hand, fecal boli were present in only 25% of the EEP-treated animals, versus 57% in the Saline treated animals. Larger sample sizes may be capable of demonstrating a statistically significant reduction in anxiety using this index.

References

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Citation	Leff, D. (2015). Effectiveness of an analog of thyrotropin-releasing hormone in alleviating PTSD, using an animal model of anxiety. *Duluth Journal of Undergraduate Research, 2*, 94-98. Permalink: http://hdl.handle.net/10792/2649
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